Claims 4-11 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**.

II. Rejection of Claims 4-11 Under 35 U.S.C. § 101

The Action first rejects claims 4-11 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

As set forth in Applicants' response mailed on March 6, 2003 ("the previous response") to the First Office Action on the merits in this case, which was mailed on November 6, 2002 ("the First Action"), the present invention has a number of substantial and credible utilities, not the least of which is in diagnostic assays, as described in the specification, at least at page 10, line 35. As described in the specification from page 7, line 37 through page 8, line 2, the present sequence defines a coding single nucleotide polymorphism - specifically, an A/T polymorphism at position 598 of SEQ ID NO:6, which can lead to an isoleucine or valine residue at amino acid position 200 of SEQ ID NO:7. As such polymorphisms are the basis for **forensic** analysis, which does not require any information at all about the ultimate biological function of the encoded protein, and is undoubtedly a "real world" utility, the present sequences must in themselves be useful.

The Examiner questions this asserted utility, stating "it does not mean that the change in amino acid will affect activity or cause a disease or condition" (Action at page 3). This argument is **completely** misinformed. Applicants respectfully point out that **forensic** analysis is used to specifically identify individual members of the human population simply based on the presence or absence of one or more polymorphisms. As set forth above, **forensic** analysis does not require **any information at all** about the ultimate biological function of the encoded protein, or require that the mutation cause a "disease or condition". Using the polymorphic marker as described in the specification as originally field, the skilled artisan can distinguish members of a population from one another without any additional research. In the worst case scenario, this polymorphic marker is useful to distinguish 50% of the population (in other words, the marker being present in half of the population). Applicants point out that the ability of a polymorphic marker to distinguish at least 50% of the population is an inherent feature of any polymorphic marker, and this feature is well understood by those of skill in the art. Applicants note that as a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988). Applicants respectfully point out that all that is required to support this assertion of utility is for the skilled artisan

to believe that the presently described polymorphic marker could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers such as that described by Applicants every day provides more than ample support for the assertion that forensic biologists would also be able to use the specific polymorphic marker described by Applicants in the same fashion. Therefore, the presently claimed sequence clearly has a substantial and well established utility. The ability to eliminate 50% of the population from a forensic analysis **clearly** is a real world, practical utility. Thus, the Examiner's argument in no way supports the allegation that the presently claimed sequence lacks a patentable utility.

Furthermore, Applicants submit that the asserted forensic utility is specific precisely because it cannot be applied to just any polynucleotide. In fact, the basis for forensic analysis is the fact that such polymorphic markers are **not** present in all other nucleic acids, but in fact specific and unique to only a certain subset of the population. Additionally, until a polymorphic marker is actually described it cannot be used in forensic analysis. Put another way, simply because there is a likelihood, even a significant likelihood, that a particular nucleic acid sequence will contain a polymorphism and thus be useful in forensic analysis, until such a polymorphism is actually identified and described, such a likelihood is **meaningless**. As set forth in the previous response, the Examiner appears to be confusing the requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, with the requirement for a **unique** utility, which is clearly an improper standard. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Importantly, the holding in the *Carl Zeiss* case is **mandatory legal authority** that essentially controls the outcome of the present case. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. All batteries have the exact same utility - specifically, to provide power. All automobile tires have the exact same utility - specifically, for use on automobiles. All golf balls and golf clubs have the exact same utility - specifically, use in the game of golf. All cancer

treatments have the exact same utility - specifically, to treat cancer. All anti-infectious agents have the exact same broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Furthermore, as the presently described polymorphisms are a part of the family of polymorphisms that have a well established utility, the Federal Circuit's holding in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the present polymorphisms are useful in forensic analysis as described in the specification as originally filed, without

the need for any further research. As discussed above, even if the use of these polymorphic markers provided additional information on the percentage of particular subpopulations that contain these polymorphic markers, this would not mean that "additional research" is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. As stated above, using the polymorphic marker as described in the specification as originally field can definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Again, as a matter of law, it is well settled that a patent need not disclose what is well known in the art (*In re Wands, supra*).

Importantly, it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As set forth in *In re Langer* (183 USPQ 288 (CCPA 1974); "*Langer*"):

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Thus, absent such evidence from the Examiner concerning the use of the presently described polymorphisms in forensic analysis, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Additionally, in the previous response, Applicants pointed out that the assertion in the specification as originally filed that the presently claimed sequence encodes a member of the platelet derived growth factor (PDGF) family (see the specification as originally filed, at least from page 2, line 34 to page 3, line 1) is supported by the fact that four sequences sharing 100% percent identity at the protein level over an extended region of the claimed sequence are present in the leading scientific repository for biological sequence data (GenBank), and have been annotated by third party scientists who are *wholly unaffiliated with Applicants* as "Homo sapiens platelet derived growth factor C" (Li *et al.*, Nat. Cell Biol. *2*:302-309, 2000 and Gilbertson *et al.*, J. Biol. Chem. *276*:27406-27414, 2001; GenBank accession numbers NM_016205 and AF260738; abstracts, alignments and GenBank reports shown in **Exhibit B**), "Homo sapiens secretory growth factor-like protein fallotein" (which is a member of the PDGF family; Tsai *et al.*, Biochim. Biophys. Acta *1492*:196-202, 2000; abstract, alignment and GenBank report shown in **Exhibit C**), and "Homo sapiens hSCDGF mRNA for spinal-cord-derived growth factor (which is also a member of the PDGF family; Hamada *et al.*, FEBS Lett. *475*:97-102, 2000; abstract, alignment and GenBank report shown in **Exhibit D**). Applicants pointed out that the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given all of these GenBank annotations, there can be no question that those skilled in the art would clearly believe that Applicants' sequence is a member of the platelet derived growth factor family. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Examiner questions this assertion of utility, stating that "the polypeptide taught by the specification will not have activity as taught by Li *et al.*" (Action bridging pages 4 and 5). However, this argument is not particularly germane to the assertion made by Applicants. Applicants provided the alignments in **Exhibits B, C** and **D**, above, to indicate the extensive homology between the presently claimed sequence and a variety of members of the platelet derived growth factor family, rather than functional identity to any of these specific members of the platelet derived growth factor family. Thus, while Applicants have provided evidence of record that conclusively establishes that those skilled in the art would believe that the specifically claimed sequence encodes a member of the platelet derived growth factor family, the Examiner has provided no evidence that directly establishes that the specifically claimed sequence does not encode a member of the platelet derived growth factor family. Accordingly, the evidence of record compels a finding that the present invention has a patentable utility.

Additionally, in the previous response, Applicants discussed the shortcomings of the three

references that the Examiner cited to support the allegation that certain proteins that have different sequences can have different functions. Specifically, the Examiner cited an article by Skolnick *et al.* ("Skolnick"; 2000, Trends in Biotech. *18*:34-39), an issued U.S. Patent to Tischer *et al.* (U.S. Patent No. 5,194,596; "Tischer"), and Yan *et al.* (2000, Science *290*:523-527; "Yan"). Applicants will not present the arguments against these references again, instead incorporating by reference the arguments set forth in the previous response in their entirety. However, with regard to the citation of journal articles to support an allegation of a lack of utility, the PTO has repeatedly attempted to deny the utility of nucleic acid sequences based on a small number of publications that call into doubt prediction of protein function from homology information and the usefulness of bioinformatic predictions, of which these articles are merely examples. Applicants readily agree that there is not 100% consensus within the scientific community regarding prediction of protein function from homology information, and further agree that prediction of protein function from homology information is not 100% accurate. However, Applicants respectfully point out that the lack of 100% consensus on prediction of protein function from homology information is completely irrelevant to the question of whether the claimed nucleic acid sequence has a substantial and specific utility, and that 100% accuracy of prediction of protein function from homology information is not the standard for patentability under 35 U.S.C. § 101. Applicants respectfully point out that, as discussed above, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be believable. Applicants submit that the overwhelming majority of those of skill in the relevant art would believe prediction of protein function from homology information and the usefulness of bioinformatic predictions to be powerful and useful tools, as evidenced by hundreds if not thousands of journal articles, and would thus believe that Applicants sequence is a member of the platelet derived growth factor family. As believability is the standard for meeting the utility requirement of 35 U.S.C. § 101, and not 100% consensus or 100% accuracy, Applicants submit that the present claims must clearly meet the requirements of 35 U.S.C. § 101.

Therefore, given the well established biological and medical relevance of platelet derived growth factor proteins, those of skill in the art would readily appreciate the importance of tracking the expression of the genes encoding the described proteins, as described at least at page 5, lines 4-7, in priority document 60/162,547, which was incorporated in its entirety by reference into the present specification as originally filed. In particular, the specification describes how the described sequences can be represented using a gene chip format to provide a high throughput analysis of the level of gene

expression. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. Applicants point out that nucleic acid sequences are commonly used in gene chip applications without **any** information regarding the function of the encoded protein, or even evidence regarding whether the sequence is actually even expressed. Thus, the present sequence, which has been biologically validated to be expressed, has a much greater utility than sequences that are merely predicted to be expressed based on bioinformatic analysis. Additionally, Applicants point out that nucleic acid sequences such as SEQ ID NO:6 are routinely used by companies throughout the biotechnology sector **exactly** as they are presented in the Sequence Listing, without **any** further experimentation. Expression profiling does **not** require a knowledge of the function of the particular nucleic acid on the chip - rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types.

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, there can be no doubt that the skilled artisan would know how to use the presently claimed sequences (see Section III, below), strongly arguing that the claimed sequences have utility. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel and potentially medically relevant* sequences would have great utility in such DNA chip applications. As the present sequences are specific markers of the human genome (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be ideal, novel candidates for assessing gene expression using such DNA chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Applicants

respectfully remind the Examiner that the requirements of a **specific** utility should not be confused with a requirement for a **unique** utility. Simply because other polynucleotide sequences can be used to track gene expression on a gene chip does not mean that the use of the presently claimed nucleic acid sequence in gene chip applications is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC*, *supra*). Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as set forth in the previous response, a further example of the utility of the presently claimed polynucleotide, as described in the specification at least at page 10, lines 34-35, the present nucleotide sequences have a specific utility in "determining the genomic structure", for example in the identification of coding sequence and mapping the gene to a particular chromosome. This is evidenced by the fact that SEQ ID NO:6 can be used to map the 5 coding exons on chromosome 4 (present within two overlapping chromosome 4 clones; GenBank Accession Numbers AC093325 and AC092608; alignments and the first page from the GenBank reports are presented in **Exhibit E**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 4 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Applicants respectfully reminded the Examiner that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence, as described above. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon

splice-junctions). The specification details that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics" (specification from page 10, line 36 to page 11, line 3). Applicants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of Venter *et al.* (2001, Science *291*:1304 at pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Action also questions these asserted utilities, stating that "any chromosome region 4 gene can be used to map that particular area of the chromosome" (Action at page 6). The Examiner once again seems to be confusing the requirements of a **specific** utility with a **unique** utility. The fact that a small number of other nucleotide sequences could be used to map the protein coding regions in this specific region of chromosome 4 does not mean that the use of Applicants' sequence to map the protein coding regions of chromosome 4 is not a specific utility (*Carl Zeiss Stiftung v. Renishaw PLC*, *supra*).

Finally, as set forth in the previous response, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have

been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section III, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, as well as the reasons sets forth in the previous response, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 4-11 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

III. Rejection of Claims 4-11 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 4-11 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 4-11 have been shown to have "a specific, substantial, and credible utility", as detailed in section II above, the present rejection of claims 4-11 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 4-11 under 35 U.S.C. § 112, first paragraph, be withdrawn.

IV. Rejection of Claims 4, 7 and 8 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 4, 7 and 8 under 35 U.S.C. § 112, first paragraph, as allegedly

not providing enablement for "fragments of polynucleotides" (Action at page 8). Applicants respectfully traverse.

In the previous response, Applicants pointed out that there is absolutely no requirement that all species of an invention must have all of the exact same properties. The Examiner apparently agrees, stating "(t)here is no requirement that all species of an invention have the exact same properties" (Action at page 8), but then goes on to question the enablement of polynucleotide fragments because "there is no assurance that when the DNA is expressed, the protein would have the desirable properties of the invention" (Action bridging pages 8 and 9). The Examiner appears to believe that the only "desirable property" that a polynucleotide fragment of the present invention could have is the specific biological properties of the full length protein encoded by SEQ ID NO:6. However, as set forth in the previous response, it is well established that the enablement requirement is met if any use of the invention (or in this case, certain species of the invention) is provided (*In re Nelson*, 126 USPQ 242 (CCPA 1960); *Cross v. Iizuka, supra*). "The enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins Univ. v. CellPro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998), citing *Engel Indus., Inc. v. Lockformer Co.*, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991). The Examiner has already conceded that SEQ ID NO:6 is enabled. Thus, the enablement issue should be resolved. Enablement only requires that the specification describe a practical use for the composition defined in the claims, and that a skilled artisan be able to make and use the claimed DNA segments without undue experimentation. Accordingly, by the Examiner's own admission, the § 112 requirement has certainly been met.

The Examiner states that "the rejected claims encompass fragments of NHP which (sic) do not have a property" (Action at page 8). This is quite simply completely false. **At the very least**, as there are no rejections against polynucleotide fragments comprising at least 24 contiguous bases of nucleotide sequence from SEQ ID NO:6, these fragments have the property of being unique identifiers of SEQ ID NO:6. Applicants point out that significant commercial exploitation of nucleic acid sequences requires no more information than the nucleic acid sequence itself. Applications ranging from gene expression analysis or profiling to chromosomal mapping are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and the enablement provided by disclosures such as the present specification, which include specific nucleic acid sequences and guidance regarding the various uses of such sequences.

As set forth in the previous response, there is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification. For example, it is not unreasonable to expect a Ph.D. level molecular biologist to be able to use the disclosed sequence to design oligonucleotide probes and primers and use them in, for example, PCR based screening and detection methods to obtain the described sequences and/or determine tissue expression patterns. Nevertheless, the present specification provides highly detailed descriptions of techniques that can be used to accomplish many different aspects of the claimed invention, including recombinant expression, site-specific mutagenesis, *in situ* hybridization, and large scale nucleic acid screening techniques, and properly incorporates by reference a montage of standard texts into the specification, such as Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*) and Ausubel *et al.* (*Current Protocols in Molecular Biology*) to provide even further guidance to the skilled artisan. Incorporation of material into the specification by reference is proper. *Ex parte Schwarze*, 151 USPQ 426 (PTO Bd. App. 1966). The § 112, first paragraph rejection is thus *prima facie* improper:

> As a matter of patent office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi & Horton, 169 USPQ 367, 369 (CCPA 1971), emphasis as in original. In any event, an alleged lack of express teaching is insufficient to support a first paragraph rejection where one of skill in the art would know how to perform techniques required to perform at least one aspect of the invention. As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra.* In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). As standard molecular biological techniques are routine in the art, such protocols do not need to described in detail in the specification.

Furthermore, a specification "need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it." *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968); emphasis added. The present claims are thus enabled as they are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

As detailed above, and in the previous response, all aspects of the enablement rejection under 35 U.S.C. § 112, first paragraph have been overcome. Applicants therefore respectfully request that the rejection be withdrawn.

V. Rejection of Claim 4 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claim 4 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

The Action states that claim 4 fails to meet the written description requirement because the specification "discloses only a structural feature" (Action at page 10). Applicants respectfully point out that this is **all that is required** for claim 4 to meet the written description requirement of 35 U.S.C. § 112, first paragraph. As set forth in the previous response, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the . . . nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

The Examiner seems to be requiring a complete and exact description of every member of the claimed genus in order to comply with the requirements of 35 U.S.C. § 112, first paragraph. Applicants respectfully point out that this is **not** the standard for compliance with 35 U.S.C. § 112, first paragraph. As clearly set forth in the *Regents of Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), the Federal Circuit stated that:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can **distinguish** such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus (emphasis added).

Thus, a claim describing a genus of nucleic acids by **structure**, formula, chemical name **or** physical properties sufficient to allow one of ordinary skill in the art to **distinguish** the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. Using the nucleic acid

sequence of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to **distinguish** the claimed nucleic acids from other materials on the basis of the specific structural description provided. Polynucleotides that comprise at least 24 contiguous nucleotides from SEQ ID NO:6 are within the genus of claim 4, while those that lack this structural feature lie outside the genus. Claim 4 thus meets the written description requirement.

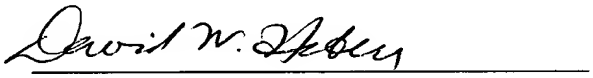
For each of the foregoing reasons, as well as the reasons set forth in the previous response, Applicants submit that the rejection of claim 4 under 35 U.S.C. § 112, first paragraph, has been overcome, and request that the rejection be withdrawn.

VI. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner DeBerry have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

October 16, 2003
Date



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